Exhibit 2

Translation of the Keizo reference

Keizo

* NOTICES *

1.This document has been translated by computer. So the translation may not reflect the original precisely.
2.**** shows the word which can not be translated.
3.In the drawings, any words are not translated.

DETAILED DESCRIPTION

[Detailed Description of the Invention]
[0001]
[Field of the Invention] This invention relates to the sugar and the lipid metabolism activator which were extracted from cleaning sesame. In detail A physic constituent or food is made to contain the extract, sesamin, or sesamol of cleaning sesame as sugar and a lipid metabolism activator. It contributes to activation of the saccharometabolism in a living body, and/or lipid metabolism by the administration or intake, and it has and is related with preventing and/or treating the disease related unusually [sugar metabolic errors, such as diabetes mellitus, hyperlipidemia, hypertension, arteriosclerosis and obesity, and/or lipid metabolism].
[0002]
[Description of the Prior Art] The onset tends [very] to be influenced by an environment, i.e., a living environment, and the lifestyle although diabetes mellitus is a disease specified hereditarily. And strong relevance is accepted between change of the lifestyle and lifestyle accompanying economical development, the obesity produced with gluttony or the lack of movement in a list, and the diabetic onset or a diabetic prevalence rate.
[0003] The fat cell in an animal tissue is storing the fat in the interior, and is performing active metabolism focusing on the saccharometabolism and lipid metabolism. The metabolic turnover depression of these cells and also a malfunction are set to one of the causes, and diseases, such as diabetes mellitus, hyperlipidemia, hypertension, arteriosclerosis, and obesity, are brought about. In order to improve this malfunction, the differentiation to the fat cell from a precursor adipose cell is promoted, and it is thought important to make a metabolic turnover active.
[0004] On the other hand, the illness prevention and the curative effect of a component which are contained in food attract attention, and also to the aforementioned diabetes mellitus or the disease of the circulatory system, although the prevention and the curative effect by the food constituent can be acquired, development is expected.
[0005]
[Problem(s) to be Solved by the Invention] This invention aims at promoting activation of the saccharometabolism and lipid metabolism by the safe component of the food origin, i.e., promoting the activity of the saccharometabolism and lipid metabolism by using the component which contains for food, in view of the above situation.
[0006]
[Means for Solving the Problem] In order to attain the above-mentioned purpose, this invention is independent, or combines the sesamin or sesamol which is one of the 1-butanol soluble fraction of the methanol soluble fractions extracted from cleaning sesame, or the active principle of its, and uses it as sugar and a lipid metabolism activator, and it offers using this activator for prevention of the disease related unusually [saccharometabolism, such as diabetes mellitus, hyperlipidemia, hypertension, and arteriosclerosis and lipid metabolism], and/or a therapy. Namely, this invention (1) the methanol soluble extracted from cleaning sesame -- and 1-butanol -- the sugar which is a meltable fraction, and lipid metabolism activator (2) The sugar and the lipid metabolism activator (3) which are at least 1 chosen from the group which consists of sesamin and sesamol Physic constituent which contains a metabolic turnover activator according to claim 1 or 2 as an active ingredient (4) The food which contains a metabolic turnover activator according to claim 1 or 2 as an additive is offered.
[0007]
[Embodiment of the Invention] Hereafter, this invention is explained to a detail. The cleaning sesame extract fraction which is the sugar and the lipid metabolism activator of this invention can be obtained as follows.

[0008] first, cleaning sesame (Kadoya Sesame Mills) -- a methanol -- using -- warming -- it extracts, flowing back. A solvent is evaporated until it hardens the obtained extract by drying. 1-butanol and water are added to this residue, and it dissolves and puts on it gently, and distributes to each class. This is divided into a butanol layer and a water layer using a separating funnel. As for this separation, it is desirable to carry out only once, in order to avoid mixing of water. The activity fraction of this invention is obtained by hardening this butanol layer by drying. Then, in a request, the ether is added, it divides into an ether meltable object and ether insoluble matter, evaporation to dryness of them is carried out, and it is respectively good also as an ether meltable fraction and an ether insoluble fraction. Each of these ether meltable fractions and ether insoluble fractions has the pharmacological activity in this invention.
[0009] Sesamol is available from SIGMA at the trade name of SESAMOL. Moreover, what was extracted by the approach indicated by JP,1961008,B may be used so that the below-mentioned example may describe.
[0010] Next, the pharmacology effectiveness which sesamin and sesamol have is explained to the cleaning sesame extract list obtained by the above approach. Mouse 3 T3-L1 fibrocyte which is a precursor adipose cell established as a cell strain in order that the extract of the cleaning sesame which is the activator of this invention may prove having the operation which activates lipid metabolism and the saccharometabolism (3 T3-L1 is said henceforth) It used and the in vitro trial was performed.
[0011] First, about the differentiation promotion operation to a fat cell from a precursor adipose cell, in order to clarify, 3 T3-L1 fibrocyte was used and examined. Generally, as compared with differentiation before, it is known for the cell which specialized in the fat cell from fibrocyte that glycerol-3-phosphoric-acid dehydrogenase (GPDH) activity rises remarkably and that the amount of intracellular triglycerides will increase similarly further. Glycerol-3-phosphoric-acid dehydrogenase (GPDH) activity and the amount of intracellular triglycerides were measured as an index of the effectiveness to the fat cell differentiation of this invention from this.
[0012] The inclination of the increment in GPDH activity and the inclination of the increment in the amount of TG were looked at by sesamin and sesamol at the ether meltable fraction and ether insoluble fraction list which are the sugar and the lipid metabolism activator of this invention.
[0013] On the other hand, the insulin also has the operation which reinforces the differentiation to a fat cell. Then, in order to examine the synergism of the activator of this invention, and an insulin, this extract, sesamin, or sesamol was respectively used together with the insulin. That is, measurement of the GPDH activity when setting to 1microM insulin concentration used together and the amount of TG was performed (Table 1). The concomitant use with the activator of this invention and an insulin guided the increment in remarkable GPDH activity, and the increment in the amount of TG as compared with the time of processing an insulin independently (Table 1). This effectiveness was more powerful than the case where the dexamethasone (0.25microM) and the 1-methyl-3-isobutyl xanthin (0.5mM) which are used as a differentiation accelerator of a precursor adipose cell, and an insulin (6microg/mL) are used together (Table 1). Sesamin and sesamol also reinforced the effectiveness of an insulin respectively (Table 1).
[0014] Next, in order to clarify a saccharometabolism improvement operation of this invention, the amount of incorporation of the glucose in 3 T3-L1 after differentiation was measured. After making 3 T3-L1 fibrocyte specialize in a fat cell using the sesamin and/or the insulin of this invention, it did not add but sesamin measured about change of the amount of glucose incorporation in 3 T3-L1 cell which set the addition group and the additive-free group and specialized about the insulin.
[0015] In 3 T3-L1 processed by sesamin, incorporation of a glucose went up remarkably by addition of an insulin. The value is a numeric value (Table 2) calculated with the difference of the existence of an insulin as effectiveness of an insulin. That is, this shows that the susceptibility of an insulin is increasing in the cell processed by sesamin.
[0016] Furthermore, the physic constituent used by this invention is explained. The physic constituent of this invention can be prevented and/or treated by the disease which activates sugar and lipid metabolism activity by the active ingredient, and is related unusually [sugar metabolic errors, such as diabetes mellitus, hyperlipidemia, hypertension, arteriosclerosis, and obesity, and/or lipid metabolism].
[0017] Although the extract, sesamin, or sesamol of this invention may be used combining oral hypoglycemic agents, such as various insulin preparation, a sulfonyl urea system, or an alpha-glucosidase inhibitor, it is not restricted to these. Although the extract of this invention promotes differentiation of a fat cell independently and activates the saccharometabolism and lipid metabolism, it has the operation which promotes an operation of an insulin powerfully by combining with an insulin.
[0018] What is necessary is just to prescribe the extract, sesamin, or sesamol of this invention for the patient by the

approach of being 1 time in the dose per day, or dividing the effective dose in within the limits of the single time dose of about 0.01mg / weight kg to about 1mg / weight kg into several times. Since a strict dosage may change with symptoms, weights, etc. of the dosage forms of an administration format and administration medicine, and the object to treat extensively, it should be determined by experience and selection of the responsible medical practitioner or veterinarian.

[0019] Although taking orally or parenteral administration, for example, administration pass and according to any paths, such as inside of the inside of the rectum, the endermic skin, hypodermically, a vein, and an urethra, intramuscular, and a nasal cavity, intraperitoneal, and an ophthalmology-path, is possible as long as an active substance is conveyed to the site of action to wish appropriately effectively, taking orally of a route of administration is desirable.

[0020] A typical physic constituent contains the active ingredient of this invention combined with the support permitted pharmacologically. In manufacture of the physic constituent of this invention, it is possible to contain the support which contains an usable excipient and an usable adjuvant for this extract pharmacologically, and it can manufacture by approach like a well-known approach, for example, idiomatic mixing, granulation, glycocalyx formation, the dissolution, or a freeze-drying process in itself. For example, it can usually mix with support, and this activity extract can be diluted by support, or can be enclosed in support. These can be added into ampul, a capsule, paper, or other containers. When using support as a diluent, a solid-state, a semisolid, or a liquid ingredient etc. with which the support can serve as a medium for this activity extract, an excipient, or a medium is applied. as suitable support -- water, salting in liquid, alcohol, a polyethylene glycol, castor oil, gelatin, a lactose, an amylose, magnesium stearate, talc, silicic acid, fatty acid monoglyceride, and a jig resaler -- although a polyvinyl pyrrolidine etc. is mentioned to the id, pentaerythritol fatty acid ester, and a hydroxymethyl cellulose list, it is not restricted to these.

[0021] A physic constituent is mixable with what kind of adjuvant, an emulsifier, the salt for osmotic-pressure adjustment, the buffer solution, a coloring agent, etc., as long as it is mixable with the activity extract of this invention harmless, if it can sterilize and is with a request.

[0022] As long as it approves as an oral agent pharmacologically, anythings, such as powder, granulation, a tablet, a sugar-coated tablet, a capsule, a soft capsule, a solution, suspension, and syrup, are possible for a physic constituent usable to an oral agent.

[0023] As long as it can use it for the suitable formula for parenteral administration as a parenteral administration agent pharmacologically, anythings, such as a water-for-injection nature solution, water-for-injection nature suspension, and suspension for oily injections, are possible.

[0024] Next, the food which can be used for this invention is explained. As for sesamin and sesamol, it is possible in the extract list of this invention to make it contain in the food of any classes and what kind of configuration as an additive which has sugar and the lipid metabolism activation effectiveness. By adding this additive, it makes it possible to use various food as health food, supplement food, nutrition fortified food, etc.

[0025] The food of this invention is contributed to constant maintenance by activating the saccharometabolism and lipid metabolism in the healthy object which took in the food of this invention by compensating the food (or food which carries out little content) which does not contain this activation component as an additive with the sugar and the lipid metabolism activation component which were extracted from the sesame which is food. For example, the disease related unusually [sugar metabolic errors such as diabetes mellitus, hyperlipidemia, hypertension, arteriosclerosis, and obesity, and/or lipid metabolism] is quietly prevented as food. it is possible for this to contribute to maintenance of health and the improvement of condition -- again If the object suffered from the disease related unusually [sugar metabolic errors, such as diabetes mellitus, hyperlipidemia, hypertension, arteriosclerosis, and obesity, and/or lipid metabolism] takes in the food of this invention Probably, by urging activation of the saccharometabolism and/or lipid metabolism, it will also be possible to assist the medical effectiveness given by a medical practitioner or the veterinarian.

[0026] The food of this invention needs to add sesamin and sesamol with an effective dose suitable as food in this sesame extract list. It is necessary to make this invention in the case of giving said object which fell ill the presentation (for example, sugar content) which does not have a bad influence on this disease so that it may be the thing of common knowledge to this contractor.

[0027] As food which can add sesamin and sesamol in this extract list Rice, legumes, wheat, wheat flour, starch, sugar, starch sugar, pans, noodles, confectionary, Edible oil, dairy products (butter, a cheese head, ice cream, lactic-acid-bacteria product, etc.), A beans product, a horticulture workpiece, soft drinks (canning, a jam, a dried fruit, fruits drink,

etc.), fermented foods and processed meat (an alcoholic beverage, vinegar, soy sauce, the source, bean paste, fermented soybeans, pickles, etc.) (a hum --) Although it is also possible for bacon, a sausage, canning, an egg product, marine foods, various frozen foods, dried foods, instant food, and pouch-packed foods to be mentioned as an example, and to add to seasonings and enzyme products, it is not restricted to these. The approach of the addition to the aforementioned food is possible by any approaches well-known to this contractor.

[0028]

[Example] Hereafter, although the example of this invention is explained, this invention is not limited to these.

Example 1: The extract <extract of active ingredient of this invention> cleaning sesame (Kadoya Sesame Mills make) of an active ingredient was extracted for 1 hour, flowing back by being on [of 80 degrees C] a water bath using the methanol of 300mL. This was performed 3 times. The obtained extract is set, and being on [of 50 to 60 degrees C] a water bath, and decompressing, using the rotary evaporator, the solvent was evaporated until this extract hardened by drying. The 1-butanol of 200mL(s) and the water of 200mL(s) were added to this residue, and it dissolved in it, and distributed to each class by putting one evening at a room temperature. This was divided into the butanol layer and the water layer using the separating funnel. The butanol layer hardened by drying, added the ether (200mL) after that, and divided it into an ether meltable object and ether insoluble matter. Evaporation to dryness of them was carried out, and it considered as the ether meltable fraction and the ether insoluble fraction respectively.

[0029] According to the indication of <extract of sesamin and sesamol> JP,1961008,B, it extracted as follows.

1. Stirring and standing separated 30g of sesame oil deordorization distillates produced at the process which extracts and refines sesame oil from a sesame raw material by the extract usual approach of sesamin within the separating funnel using 60% ethanol water-solution 300mL, and centrifugal separation of the upper ethanol-water mixed liquor 280mL was carried out. The glass column with a diameter [of 2.5cm] and a die length of 50cm was filled up with 80g (BET surface area; more than 5m2/g pore volume; 0.05 or more mL/g, the ORGANO CORP. make, EP- 3211) of adsorbents of the porosity which uses the polymer of trimethylolpropane trimethacrylate as a principal component, said upper ethanol-water mixed liquor 280mL was applied, the non-adsorbing component was completely flushed with the ethanol water solution 60%, and the effluent containing a non-adsorbing component was extracted. Then, the adsorption component was eluted in the eluate of ethanol 100%, ethanol was distilled off, and sesamin was obtained as brown oily matter and solid mixture (yield of 80%, yield of 0.702g).

[0030] 2. After having used the extract approach styrene divinylbenzene copolymer of sesamol as the base material, filling up the with a diameter die length [50cm die length of 2.5cm] glass column with 70g (loam and the product made from HASU; Amberlite IRA-401) of I-beam strong base nature ion-exchange resin of a low degree of cross linking with which the 4th class amine was combined with this and using said ion-exchange resin as OH mold by NaOH further, it let ethanol pass 60% in said column. The effluent extracted at the time of the extract of said sesamin was applied there, non-adsorbing liquid was flushed, the adsorption component was eluted in methanol solution 400mL which dissolved 12g boric acid, and sesamol was obtained as brown oily matter and solid mixture by distilling off a methanol (yield of 92%, yield of 0.593g).

[0031] Example 2: Culture mouse 3 T3-Lof pharmacological action 1. mouse 3 T3-L1 fibrocyte1 fibrocyte is Howard. It received from Green (Massachusetts Institute of technology) and cultivated within the incubator of 37 degrees C and 5%CO2 with 35mm culture plate (Nunc make) using the Dulbecco's modified Eagle's medium (NISSUI PHARMACEUTICAL [CO., LTD.] make: 10% fetal calf serum, penicillin (50 U/mL), streptomycin (50microg/mL) content). Culture-medium exchange was performed once on 2 to the 3rd. When seeding was carried out to 35mm culture plate by 1x104 cells/mL, it became confluent in six days. The cell which became confluent was used for the experiment.

[0032] 2. By Approach to Have Carried Out Measurement Above-mentioned of Glycerol-3-Phosphoric-Acid Dehydrogenase (GPDH) Activity and the Amount of Intracellular Triglycerides To 3 T3-L1 which carried out seeding to 35mm culture plate, cultivated for six days, and became confluent 1microM insulin prepared by the culture medium used at the time of the culture of 3 T3-L1 mentioned above (SIGMA company make), 1microM insulin and 1microg/mL - 100microg/mL ether meltable fraction, The insulin of 1microM, and the ether insoluble fraction of 1microg/mL - 100microg/mL, The insulin of 1microM and the sesamin of 3micro M-100microM, the insulin of 1microM, and the sesamol of 3micro M-30microM, The mixture of 6microg/mL insulin was added in 0.25microM dexamethasone and the 1-methyl-3-isobutyl xanthin list of 0.5mM(s) (concentration is the last concentration respectively), and it cultivated by 37 degrees C and 5%CO2 for ten more days. It collected after two washing by 0.9%

NaCl ice-cooled after that, and suspended in the 1mMEDTA content 25mM tris-HCl buffer solution (pH7.5). The homogenate of this cell suspension was carried out with the supersonic wave (Tietech make), and it carried out centrifugal at 4 degrees C for 20 minutes by 8000xg. The obtained supernatant liquid was used for measurement of glycerol-3-phosphoric-acid dehydrogenase activity, and measurement of the amount of intracellular triglycerides.

[0033] Measurement of glycerol-3-phosphoric-acid dehydrogenase activity measured reduction of the absorbance in 340nm by oxidation of NADH at 23 degrees C, using dihydroxyacetone phosphate as a substrate (K et al.-hytotherapy research, vol1, No 2 and 1987). [Sekiya,]

[0034] The triglyceride assay kit made from WAKO was used for the measuring method of the amount of intracellular triglycerides. The amount of proteins in the sample measured with the Lowry method amended each data. Moreover, the experiment was conducted 3 times by the duplicate and the typical data was shown (Table 1).

[0035]

[Table 1]

表 1

ゴマ関連物質による前駆脂肪細胞分化促進作用

試料	GPDH (%)	TG (%)	試料	GPDH (%)	TG (%)
None	18. 7	58. 9	None	14. 1	31. 3
Ins (コントロール) *	100	100	Ins (コントロール)	100	100
DMI **	279	224	DMI	240	265
Ins+エーテル可溶 1μg/mL	101	106	Ins+セサミン 3μM	120	95. 8
Ins+エーテル可溶 10μg/mL	146	130	Ins+セサミン 10μM	119	100
Ins+エーテル可溶 100μg/mL	812	583	Ins+セサミン 30μM	185	169
Ins+エーテル不溶 1μg/mL	99. 5	124	Ins+セサミン 100μM	292	273
Ins+エーテル不溶 10μg/mL	80. 9	153	Ins+セサモール 3μM	115	97. 9
Ins+エーテル不溶 100μg/mL	152	436	Ins+セサモール 10μM	140	108
Ins+水層 1μg/mL	122	141	Ins+セサモール 30μM	157	121
Ins+水層 10μg/mL	158	135			
Ins+水層 100μg/mL	139	147			

＊Ins： インスリンにも脂肪細胞の分化促進効果があり、測定を容易にするためインスリンを添加したものをコントロールとし、それに対する比率を出した。

＊＊DMI： デキサメタゾン、メチルキサンチン、インスリンの混合物。前駆脂肪細胞の分化促進剤。

[0036] The rate (%) of the GPDH activity in each processing cell or the amount of intracellular TG when making into 100% the GPDH activity or the amount of intracellular TG in the cell which carried out 1microM insulin processing showed the numeric value of Table 1.

[0037] Although promotion of GPDH activity and the increment in the amount of intracellular TG are not necessarily parallel, since both both are the indexes of differentiation, it is thought that differentiation is guided whichever the value is rising.

[0038] By the <measurement of amount of glucose incorporation> aforementioned culture approach, carry out seeding to 35mm culture plate, and it cultivates for six days. 1microM insulin and/or 3micro M-100microM sesamin (concentration is the last concentration respectively) which were prepared by the culture medium used for 3 T3-L1 fibrocyte which became confluent at the time of the culture of 3 T3-L1 mentioned above were added, and it cultivated by 37 degrees C and 5%CO2 for ten more days. Differentiation began from the time of 3 T3-L1 fibrocyte adding an insulin and/or sesamin respectively. It washed twice ten days after by the culture medium which does not contain an insulin or sesamin, and the same culture medium as what was used for this washing was added, it cultivated before or after ten more days, and the amount of glucose incorporation was measured.

[0039] While adding 1microM insulin, 74KBq addition only of the glucose which carried out the indicator of the glucose which carried out the indicator by 14C by 74KBq addition or 14C was carried out, and it put on 3 T3-L1 washed twice by the aforementioned culture medium gently at 37 degrees C for 30 minutes. Next, the phosphate buffer solution which removed supernatant liquid and was ice-cooled washed twice, and the cell was dissolved with SDS and alkali. The triglyceride was extracted by the heptane and isopropyl alcohol and each activity activity was measured for this extracted triglyceride with the scintillation counter.

[0040] The amount of proteins in the sample measured with the Lowry method amended each data. Moreover, the experiment was conducted 3 times by the duplicate and the typical data was shown (Table 2).
[0041]
[Table 2]
表 2
セサミンによるグリコース取り込み促進

試料	グルコース取り込み時のインスリン（1μM）の有無	取り込まれたグルコース量＊ (fmol/mg protein)	インスリンの効果＊＊ (有−無)	(%)
コントロール	無	2. 88±0. 27	5. 6	100
	有	8. 49±0. 33		
3μM セサミン	無	3. 38±0. 58	6. 6	118
	有	9. 96±0. 24		
10μM セサミン	無	2. 57±0. 09	7. 5	184
	有	10. 09±1. 00		
30μM セサミン	無	3. 78±0. 65	14. 6	261
	有	18. 42±5. 64		
100μM セサミン	無	5. 34±0. 29	22. 7	405
	有	28. 06±1. 40		

基本培地にはインスリンを添加した。
＊平均値±標準偏差で表示
＊＊取り込まれたグルコースのインスリンの有無による差、対照を１００%としたときの値

[0042] The numeric value of Table 2 showed the incorporated amount of glucoses in fmol/mg protein. The following thing was checked from the above result. Sesamin and sesamol promote notably differentiation by the insulin of 3 T3-L1 fibrocyte which is a precursor adipose cell in the extract list of the cleaning sesame of this invention. The capacity of 3 T3-L1 which specialized which accumulates a fat improves, and it can consider possibility that sesamin and sesamol will activate lipid metabolism in the extract list of this invention, by this. Furthermore, susceptibility [as opposed to an insulin in 3 T3-L1 which specialized by sesamin] increased, and it was suggested that the saccharometabolism in intracellular is activated by it. Sesamin and sesamol were considered that possibility that it can be used for prevention and the therapy of diabetes mellitus, hyperlipidemia, hypertension, arteriosclerosis, etc. is high by the above at the extract list of this invention.
[0043] As mentioned above, although this invention was fully explained, this contractor will understand easily that the same effectiveness is acquired, without deviating from the range of this invention, even if it changes the conditions and formula which were indicated in the above-mentioned example.